

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

Appl. No.	:	09/674,962	Conf. No.	:	7018
Appellant	:	HAUER, Bernhard	Filed	:	Nov. 8, 2000
Examiner	:	WESSENDORF, Teresa	TC/A.U.	:	1639
Docket No.	:	49041	Customer No.	:	26474

Mail Stop Appeal Brief  
Commissioner for Patents  
P.O. Box 1450  
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**BRIEF ON APPEAL**

(37 C.F.R. §41.37)

Honorable Sir:

This Appeal Brief is submitted in response to the Final Office Action of February 27, 2007 and Advisory Action of July 24, 2007.

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Inventor: HAUER, Bernhard  
Docket No.: 49041

#### REAL PARTY IN INTEREST

The real party in interest is BASF Aktiengesellschaft, of Ludwigshafen, Germany, as recorded on November 8, 2000 at Reel/Frame 011830/0340.

#### RELATED APPEALS AND INTERFERENCES

There are no related appeals and interferences currently pending. A Decision on Appeal in the above-identified application was mailed by the USPTO on April 28, 2006 (Appeal No: 2005-2596).

#### STATUS OF CLAIMS

Claims 5-9 are currently pending and are currently rejected under 35 USC § 103(a). Claims 1-4 are canceled.

#### STATUS OF AMENDMENTS

The claims have not been amended subsequent to the final rejection.

#### SUMMARY OF CLAIMED SUBJECT MATTER

The invention described by Claim 5 relates to a novel peptide comprising SEQ ID NO: 1 wherein the variables X1 to X6 are defined by the following amino acids:

X1= Asn;

X2= Gln, Glu or Arg;

X3= Gly, Thr or Tyr;

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X4= Asn or Arg;

X5= Gly or Lys; and

X6= Cys.

(See Specification page 3, line 9 – page 4, line 17). The invention described by Claim 6 relates to a peptide fragment having SEQ ID NO: 3 (See Specification, page 5, line 25). The invention described by Claim 7 relates to a peptide fragment having SEQ ID NO: 3 (See Specification, page 5, line 27). The invention described by Claim 8 relates to a peptide fragment having SEQ ID NO: 4 (See Specification, page 5, line 29). The invention described by Claim 9 relates to a peptide fragment having SEQ ID NO: 5 (See Specification, page 5, line 31).

Each of SEQ ID NOS: 1-5 relate to novel peptide fragments which serve as protein tags for IMAC, which exhibit increased protein selectivity and simplification of protein purification (Specification page 3, lines 1-7).

#### GROUND OF REJECTION TO BE REVIEWED ON APPEAL

Whether claims 5-9 are obvious under 35 U.S.C. 103(a) in view of Volz et al. (Journal of Chromatography), Guerinot et al. (U.S. Patent No. 5,846,821) and Haymore et al. (EP 409,814).

#### ARGUMENT

##### The Rejection of Claims 5-9 under 35 U.S.C. §103(a)

Claims 5-9 stand rejected under 35 U.S.C. § 103 (a) as allegedly unpatentable over Volz et al. (Journal of Chromatography) in view of Guerinot et al. (U.S. Patent No. 5,846,821) and Haymore et al. (EP 409,814). The Office Action of February 27, 2007 alleges that “it would

have been obvious to one having ordinary skill in the art at the time of the invention to pick and choose from the 20 naturally occurring amino acid, the ones that can occupy the x positions in the peptide sequence motif of Volz. Haymore, Guerinot and Volz all disclose that the amino acids at the non-critical or intervening residues between the His and Cys metal binding residues are relatively unimportant in the binding of peptide fragments to metals." (Emphasis added). Appellant respectfully traverses the rejection.

1.) The Combination of the References Fails to Disclose Each and Every Element of the Claimed Invention to Support a *Prima Facie* Case of Obviousness.

Appellant respectfully submits that the combination of the references fails to teach each and every element of the claims to support a prima facie case of obviousness. The Examiner asserts that Volz et al. describes a peptide fragment of formula HXHXHXXCXXC (SEQ. ID NO:1) in which Leu is present in the position of the peptide fragment corresponding to X<sup>3</sup>, and any of the 20 naturally-occurring amino acid residues in the positions of variables X<sup>1</sup>-X<sup>6</sup>. The Examiner further asserts the pending claims place Ile where Volz et al. place Leu and that based on teachings of Guerinot et al. and Haymore et al., Leu and Ile can be substituted for each other without losing metal binding properties. However, none of the pending claims recite peptides containing Ile in X<sup>3</sup> position. Notwithstanding, the Examiner asserts, in the Response to Arguments section (Page 4), that "although none of the claims recite Ile, it does not obviate the finding of obviousness that any of the 19 amino acid residues, besides Ile can occupy the X positions, as taught by the references." However, as discussed, *infra*, such statement and random substitution is wholly contrary to the principles of the claimed invention, which is directed to

providing novel peptide fragments that exhibit increased protein selectivity and simplification of protein purification when compared with known fragments. (Specification page 3, lines 1-7).

2.) Conservative Amino Acid Substitutions Cannot Be Applied to All Substitutions

The Examiner asserts Guerinot et al. (U.S. Patent No. 5,846,821) describes that conservative amino acid residues (e.g. Leu and Ile) can be substituted for one another, especially in “non-essential” positions such that it would have been obvious to one having ordinary skill in the art at the time the invention was made “to pick and choose from the 20 naturally occurring amino acid[s], the ones that can occupy the x positions in the peptide sequence motif of Volz.” However, Appellant respectfully submits that such positions are essential such that Appellants claimed substitutions in such positions supports the non-obviousness of the instant claims.

Additionally, in arguing the Examiner’s general assertion regarding conservative amino acid substitutions, Appellant submits that Guerinot et al. specifically states that, “[a] “conservative amino acid substitution” is one in which the amino acid residue is replaced with an amino acid residue having a similar side chain.” (column 14, lines 18-21) (Emphasis added). Accordingly, Guerinot et al. defines families of amino acid residues having similar side chains; wherein the family of “non-polar” side chain amino acids is defined to include alanine, valine, leucine, isoleucine, proline, phenylalanine, methionine, and tryptophan. (column 14, lines 21-30) (Emphasis added). Additionally, Guerinot et al. concludes “a predicted nonessential amino acid residue...is preferably replaced with another amino acid residue from the same side chain.” (column 14, lines 30-33) (Emphasis added). Consequently, contrary to the Examiner’s assertion, there is simply no teaching or suggestion to substitute an amino acid of one side chain

family with an amino acid from another side chain family or to simply pick and choose from among the 20 naturally occurring amino acids for each of positions  $X^1$ - $X^6$ . “The fact that a claimed species is or subgenus is encompassed by a prior art genus is not sufficient by itself to establish a *prima facie* case of obviousness.” *In re Baird*, 16 F.3d 380, 29 USPQ2d 1550 (Fed. Cir. 1994). “The fact that a claimed compound may be encompassed by a disclosed generic formula does not by itself render that compound obvious.” *Id.*, citing *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). “A disclosure of millions of compounds does not render obvious a claim to three compounds, particularly when that disclosure indicates a preference leading away from the invention.” *Id.*

Furthermore, while the Board of Patent Appeals & Interferences Decision stated that, “the only difference between the prior art peptide fragment and the [claimed] peptide fragment...is a Ile residue at position  $X^3$  instead of a Leu residue, we agree with the [E]xaminer that it would have been obvious to one of ordinary skill in the art to construct a peptide fragment having the claimed conservative amino acid substitution (i.e., a peptide fragment wherein  $X^3$  is a Leu residue),” (page 5, lines 16-18) and further indicated that Guerinot et al., “merely provides evidence of the correctness of the Examiner’s position that these two amino acids are functional equivalents,” referring to Ile and Leu (page 6, lines 14-15), Appellant respectfully submits that claims 5-9 were amended subsequent to the Decision such that they do not recite “non-polar” side chain amino acids, such as Ile, for position  $X^3$ . Rather, Appellant respectfully submits that claims 5-9 recite that position  $X^3$  comprises one of “uncharged polar” side chain amino acids glycine, threonine, and tyrosine. At least according to Guerinot et al., amino acids in “non-polar” and “uncharged polar” families are not regarded as conservative substitutions. (column

14, lines 18-30).

Accordingly, there is no teaching, suggestion or motivation to undertake a “conservative” amino acid substitution and replace a non-polar amino acid with a polar amino acid. Similarly, the Examiner’s assertion that any of 20 naturally occurring amino acids may be substituted for one another is unfounded, is contrary to the teachings of the cited prior art references and is not supported prior Decision of the Board of Patent Appeals & Interferences.

3.) The Prior Art Suggests Non-Obviousness & Teaching Away

The Examiner asserts that Haymore et al. (page 4, lines 10-13) confirms the suggestion by Volz et al. that the intervening amino acids denominated as “X” are not critical to the metal binding activity of the peptide. The Examiner further asserts that Haymore et al. (page 17, lines 14-15) states the intervening residues (“X”) are not important. To characterize the teachings of Haymore et al. would be to conclude that at the time of the reference, such intervening amino acid residues were not considered critical to metal binding activity. Hence, applying the Examiner’s rationale, it would be not have been obvious for one of ordinary skill in the art at the time of the invention to substitute any of the intervening amino acids denominated as “X”. Indeed, absent from Haymore et al. is a suggestion or motivation to perform any of the claimed substitutions on intervening residues whatsoever. Therefore, the reference fails to support the Examiner’s obviousness conclusion. In fact, further analysis of Haymore et al., as directed by the Examiner, leads one of ordinary skill in the art to conclude the exact opposite, thatt is, according to Haymore et al., substitution of an intervening amino acid denominated as “X” would result in no change in the metal binding activity of the peptide. Appellant respectfully

submits that the prior art, thus, actually suggests that any attempt to substitute an intervening amino acid denominated by “X” would yield no material effect metal binding properties and would be futile in nature. Accordingly, there is simply no teaching, suggestion or motivation in Haymore et al. to undertake the claimed substitutions. Furthermore, the claimed invention proceeds contrary to the accepted wisdom in the art, which serves as strong evidence of nonobviousness. *In re Hedges*, 783 F.2d 1038, 228 USPQ 685 (Fed. Cir. 1986)

4.) Absence of Teaching, Suggestion, and Motivation to Combine Prior Art

While Appellant appreciates that “[t]he obviousness analysis cannot be confined by a formalistic conception of the words teaching, suggestion, and motivation, or by overemphasis on the importance of published articles and the explicit content of issued patents[.]” the U.S. Supreme Court has made clear that an inquiry into whether there was “...a teaching, suggestion, or motivation to combine known elements [provides] a helpful insight.” *KSR Int’l v. Teleflex, Inc.*, 550 U.S. \_\_\_\_ (2007). Such an inquiry helps to uphold the well-settled principle that an invention “composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art.” *Id.*

In view of the above, Appellant respectfully submits that the Examiner has attempted to render the instant claims obvious, “merely by demonstrating that each of its elements was, independently, known in the prior art” and by using hindsight reconstruction to use “that which the inventor taught against its teacher.” *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F2d 1540 (Fed Cir 1983). In this regard, Volz et al. (Journal of Chromatography), Guerinot et al. (U.S. Patent No. 5,846,821), and Haymore et al. (EP 409,814) do not disclose or suggest to one



of ordinary skill in the art a desirability of substituting the claimed intervening amino acid residues in order to positively effect metal binding activity of the peptide. Guerinot et al. is directed to “conservative” amino acid substitutions (column 14, lines 18-30) of isoleucine with leucine (non-polar side chain), which when considered in combination with Volz et al. Guerinot et al. does not teach, suggest or motivate one to substitute non-polar side chain amino acid residues with uncharged polar side chain amino acids, as taught by Appellant. Accordingly, it more appears that the Examiner has used hindsight reconstruction and the Appellant’s very own disclosure “as a blueprint to reconstruct the claimed invention from the isolated teachings of the prior art,” since the “expressed motivation” to make the combination is lacking from the individual references and does not emanate from that knowledge generally available to the skilled artisan. *Grain Processing Corp. v. American Maize-Prods. Co.*, 840 F.2d 902 (Fed. Cir. 1988). In this regard, while Haymore et al. may be directed to variant peptides having at least one metal-chelating amino acid sequence, Haymore et al. describes that the modification of intervening amino acid residues (“X”) is unimportant (page 3, lines 17-27; and page 4, lines 10-11). Consequently, the skilled artisan would not be motivated to make the claimed substitutions, thereby rendering the instant claims nonobvious. Therefore, the possible sources of motivation to combine references: 1) the nature of the problem to be solved; 2) the teachings of the prior art; or 3) the knowledge of persons of ordinary skill in the art, are not satisfied. *In re Rouffet*, 149 F.3d 1350, 1357, 47 USPQ2d 1453, 1457-58 (Fed. Cir. 1998).

Beyond the “teaching, suggestion, and motivation” test, the Supreme Court suggested further inquiry regarding: 1) whether the problem is recognized by one of ordinary skill in the art; 2) whether the references applied are obvious to use beyond the primary purpose; 3) whether

it would be obvious to try; and 4) whether “common sense” would make the invention apparent. *KSR Int'l v. Teleflex, Inc.*, 550 U.S. \_\_\_\_ (2007). Applying the above considerations to the instant case, it is, first, readily clear that Appellant has identified the problem of increased protein selectivity and simplification of protein purification (page 3, lines 1-7 of the instant application), which problem was not recognized by one of ordinary skill in the art. Second, the primary purpose of the invention of Guerinot et al. is directed to improvements of metal-regulated transporters and uses therefor (e.g. transgenic plants) and does not describe or suggest obvious uses beyond its primary purpose. Third, none of the prior art or the references cited by the Examiner render it “obvious to try” to combine the prior art to create the claimed invention—especially in view of the fact that the cited art teaches not to try (e.g. Guerinot et al. & Haymore et al.). Lastly, “common sense” does not direct the skilled artisan to fit the teachings of the prior art together like pieces of a puzzle since the teachings of Haymore et al. indicates amino acid substitutions of intervening amino acid residues (“X”) are unimportant and the teachings of Guerinot et al. indicates only “conservative” substitutions of the same side chain family are capable of replacement.

Accordingly, it is seen that the explicit and implicit teachings of the prior art references do not disclose, teach or suggest that substitution of the intervening amino acid residue “X” would be a desirable modification to increase the metal binding activity of the peptide. Further, it is not reasonably apparent that such modification emanates from that knowledge generally available to the skilled artisan or “common sense.” [T]here must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness.” *KSR Int'l v. Teleflex, Inc.*, 550 U.S. \_\_\_\_ (2007)

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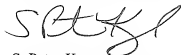
Consequently, for at least the reasons set forth above, Appellant respectfully submits that Volz et al. (Journal of Chromatography) in view of Guerinot et al. (U.S. Patent No. 5,846,821) and Haymore et al. (EP 409,814) fails to disclose or suggest each and every feature of claims 5-9 as required to support a *prima facie* case of obviousness.

The rejection should be withdrawn.

#### CONCLUSION

In view of the foregoing, Appellant respectfully asserts that claims 5-9 are nonobvious. Please charge any shortage in fees due in connection with the filing of this paper, including extensions of time, to Deposit Account No. 14-1437

Respectfully submitted,  
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CLAIMS APPENDIX

1-4 (Canceled)

5. (previously presented) A peptide comprising SEQ ID NO:1, in which the variables  $X^1$  to  $X^6$  have the following meanings:

$X^1$ = Asn;

$X^2$ = Gln, Glu or Arg;

$X^3$ = Gly, Thr or Tyr;

$X^4$ = Asn or Arg;

$X^5$ = Gly or Lys;

$X^6$ = Cys.

6. (previously presented) A peptide comprising the sequence of SEQ ID NO: 2.

7. (previously presented) A peptide comprising the sequence of SEQ ID NO: 3.

8. (previously presented) A peptide comprising the sequence of SEQ ID NO: 4.

9. (previously presented) A peptide comprising the sequence of SEQ ID NO: 5.

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EVIDENCE APPENDIX

None

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RELATED PROCEEDINGS APPENDIX

None Pending. A Decision on Appeal in the instant application was mailed on April 28, 2006 (Appeal No: 2005-2596) and is attached.